State of Alaska Epidemiology **Bulletin**

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Tuberculosis Update: LTBI Therapy and TB PCR Testing

Introduction

In 2011, Alaska had the highest incidence of tuberculosis (TB) in the nation (9.3 per 100,000 population).[1] Whereas the majority of newly identified TB cases in the United States occur in the foreign-born population, most new TB cases in Alaska are locally-acquired, and occur primarily in the Alaska Native population.[2] As a corollary, much of Alaska's prospective TB burden resides in those who currently have latent TB infection (LTBI), as 5%–10% of LTBI patients progress to active TB without therapy.[3] Thus, effective diagnosis and treatment of both active TB and LTBI are vital components of a comprehensive TB elimination strategy.

This *Bulletin* provides an update on two aspects of TB care — a new 12-week, directly observed therapy (DOT) regimen for LTBI, and a polymerase chain reaction (PCR) test for rapid diagnosis of active TB available through the Alaska State Public Health Laboratory (ASPHL).

LTBI Treatment Update

Traditional therapy for LTBI is 9 months of daily isoniazid. This regimen is simple and inexpensive. With good adherence, isoniazid therapy is highly effective at preventing active TB infection. However, this regimen is typically self-supervised, and the lengthy duration of therapy makes adherence a challenge, particularly for certain high-risk individuals. To underscore this, nationally, fewer than half of those who start an LTBI regimen complete treatment.[3]

In December 2011, the U.S. Centers for Disease Control and Prevention (CDC) recommended a new 12-week LTBI treatment option that consists of weekly DOT with isoniazid (INH) and rifapentine (RPT).[4] *This short course INH-RPT regimen is as effective as 9-month INH monotherapy, and is approved for non-pregnant patients aged ≥12 years who have LTBI and are not on antiretroviral therapy*.[4]

Three LTBI regimens are currently endorsed by CDC (Table 1). Compared with the current LTBI monotherapy options, the likelihood of successfully completing the INH-RPT regimen is substantially higher due to its shorter treatment duration and requirement for weekly DOT. Although INH-RPT has a marginally higher risk of minor drug reactions, it is associated with fewer serious adverse events than traditional INH therapy.[4] Furthermore, while INH-RPT is comparatively costly (~$200 per drug course versus ~$20 for 9 months of INH) and demands additional resources for DOT, it is likely to result in cost-effective outcomes by increasing LTBI therapy completion rates and consequently decreasing the burden of active TB in the population.[4]

Table 1: Latent TB Infection Treatment Regimens*

Regimen	Interval	Dose	Duration
INH	Daily	Adult: 5 mg/kg (max 300 mg)	9 mo
		Peds: 10–15 mg/kg (max 300 mg)	
	Twice weekly†	Adult: 15 mg/kg (max 900 mg)	
		Peds: 20–30 mg/kg (max 900 mg)	
RIF	Daily	Adult: 10 mg/kg (max 600 mg)	4–6 mo±
		Peds: 10–20 mg/kg (max 600 mg)	
INH-RPT**	Once weekly†	INH: 15 mg/kg (max 900 mg) plus RPT: 750 mg, for wt 32.1–49.9 kg 900 mg, for wt ≥50 kg	3 mo (12 wk)

INH = Isoniazid; RIF = Rifampin; RPT = Rifapentine
**For drug-susceptible LTBI (contact SOE if concern for resistance)*
†*Requires Directly Observed Therapy (DOT)*
±*Pediatric patients: 6 month course; Adults: 4 month course*
***Age <12 yrs requires approval and monitoring by a TB specialist*

TB PCR Test Update

Acid-fast bacilli (AFB) culture, the diagnostic gold standard for active TB, provides important strain and susceptibility information for clinical and public health purposes. However, culture can require up to 6 weeks for *Mycobacterium tuberculosis* to grow; this may delay treatment in the setting of clinical uncertainty or concern for potential drug toxicity. Nucleic acid amplification testing (NAAT) was developed as a rapid diagnostic test for active TB. Since December 2011, ASPHL has performed NAAT using PCR with a 24–48 hour turnaround time.[5]

ASPHL routinely performs PCR testing on all initial AFB smear-positive respiratory specimens, and will test smear-negative respiratory or non-respiratory specimens if pre-approved by the Section of Epidemiology (SOE). A positive PCR test meets the CDC case definition for lab-confirmed TB; however, providers should use clinical judgment when interpreting a negative PCR test (Table 2).[6,7] When clinically suspected, TB should not be ruled out based exclusively on a negative PCR test. In such circumstances, providers should await culture results to help guide further decision making.

Table 2: TB PCR Test Interpretation

AFB Smear	PCR Result	Interpretation
Positive	Positive	Confirmed TB
	Negative	Use clinical judgment pending culture results -- may be non-TB mycobacterium
Negative	Positive	Confirmed TB
	Negative	Use clinical judgment pending culture results -- may be false negative, but if low suspicion, likely not TB

Recommendations

1. Health care providers should consider the 12-week INH-RPT regimen for LTBI patients who have no contraindications, especially in those who are at risk for non-adherence to traditional 9-month INH monotherapy.
2. Providers should contact SOE to obtain medications and to facilitate mandatory DOT for the INH-RPT regimen.
3. Providers should contact SOE to arrange PCR testing at ASPHL for AFB smear-negative respiratory specimens or for non-respiratory specimens when TB is suspected (note: a laboratory fee may apply).
4. Providers should promptly report all suspected or confirmed active TB cases to SOE at (907)269-8000.

References

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